Half a Century of International Control Of the Venereal Diseases

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IN INTERNATIONAL negotiations to develop acceptable quarantine regulations, with which the international health movement was primarily occupied for many decades, venereal disease was of little importance. It was cholera and plague, smallpox, yellow fever, and typhus which engaged the principal attention of governments in their dealings with one another on health questions. Until after 1910, emphasis in international discussions of syphilis was often placed upon its social rather than its medical aspects, partly, perhaps, because of the poverty of preventive and therapeutic knowledge.

By the time the Health Organization of the League of Nations came into being, however, knowledge of the diagnosis and treatment of this disease had grown enormously. And as broader collaboration in health matters developed among nations, syphilis came to be recognized as a widespread and serious health problem. The Health Organization established an expert committee on syphilis, and from this group stemmed much of the useful work sponsored by the League in studying and standardizing certain venereal disease control procedures and techniques developed in the first decades of the 20th century.

In a somewhat different area, the International Union Against the Venereal Diseases also began its work in the years just after World War I. At this time, many nations began campaigns and programs against venereal disease, employing varied methods and approaches. The International Union has attempted to foster these programs and to generate support for venereal disease control nationally and internationally.

Both of these organizations, the League and the International Union, participated in a movement to provide venereal disease control services for merchant seamen. The result of this movement was the Brussels Agreement of 1924, a landmark in international venereal disease control and still an effective instrument for providing venereal disease treatment facilities for seamen.

Since World War II, the keystone of international venereal disease control has been the venereal and treponemal disease program of the World Health Organization. The modern concept of international health efforts, that of assisting nations to improve health services and conditions internally, has been given broad application in the venereal disease program, which includes training of personnel, provision of demonstration teams, exchange of scientific knowledge, and mass application of antibiotic therapy in areas of high treponemal disease prevalence.

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Antiquity of Syphilis

One of the classic controversies of medical history centers about the origin of syphilis: Whether it was brought to Europe from the New World at the close of the 15th century or existed there in antiquity. Whichever theory is correct, syphilis apparently was present in Europe

at least by 1495. An epidemic of the disease in malignant form is usually said to have swept the continent at about that time, striking first in France, Spain, and Italy, and spreading quickly to Germany and Switzerland. Holland, Greece, and England knew it in 1496; Hungary and Russia in 1499. It is said to have ranged to the Far East early in the next century (*1*, *2*).

Some writers believe that instead of a virulent syphilis racing across Europe after 1493, one or several infectious diseases, perhaps in combination with syphilis, were confused with and designated as the latter, thus giving rise to the "epidemic of syphilis" theory so often cited (*3*).

If the epidemic of about 1500 was indeed syphilis, the disease began to change within the following 50 years and has not since assumed the same violence and rapid fatality. Probably because it did not compare in virulence with such diseases as cholera and plague, syphilis did not figure prominently in later discussions of quarantine regulations designed to prevent the spread of disease from country to country (*4–6*).

Collaboration in Health

Nevertheless, in the 19th century particularly, debates and negotiations among nations on the subject of quarantine indirectly affected the development of international venereal disease control measures.

The 19th century was a time of progress in shipping and transport and consequently of growing trade and travel. Nations were drawn into closer and more diverse relationships, creating common problems calling for cooperative action. Yet, machinery through which national spokesmen could debate or act together on technical matters was lacking. In this situation, nations turned to the international conference. "When a problem became particularly acute," says Boudreau (*7*) of this period, "a government took upon itself the responsibility of calling an international conference . . ." The French Government called the First International Sanitary Conference in 1851, primarily to thrash out problems of quarantine and to seek unity in the prevention of cholera and plague. This conference represented the beginning of cooperation among nations in the field of health and sanitation. In the next half-century, a score of conferences dealt with typhus, smallpox, and yellow fever as well as cholera and plague, and in 1907 the Office Internationale d'Hygiéne Publique was established as a permanent international health office, concerned chiefly with enforcement and revision of the international sanitary conventions (*6*, *8*, *9*).

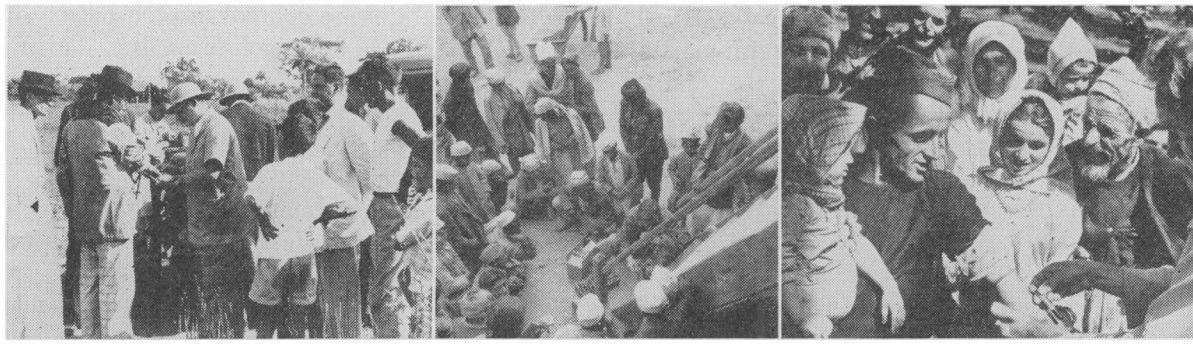
Once established, the principle of collaboration in health matters never died. Eventually, it was applied to the problem of venereal disease.

Approaches to VD Control

Before 1910, many countries confined their syphilis control efforts to regulation or repression of prostitution. Internationally, likewise, when venereal disease was discussed it was often closely identified with broad social issues rather than with health per se.

Yet, the importance of syphilis as an international health problem began to emerge at least toward the end of the 19th century. In 1899, an International Conference on the Prophylaxis of Syphilis was held at Brussels; in 1902, a second conference on the same subject, also held at Brussels, recommended among other things free treatment for all persons infected with venereal disease and distribution of leaflets emphasizing its dangers to persons entering the armed forces. Various groups, for example, the League of Red Cross Societies, the International Labour Office, and the International Union Against the Venereal Diseases, later held meetings which approached venereal disease as either a medical or a social problem or both.

The latter organization, the International Union, merits a special word as a voluntary organization with a continuous record of service. After World War I, many countries began campaigns against venereal disease; approaches and methods varied, however, and results were uneven. Speaking in 1928 of the disparity in modes of attacking the venereal disease problem, Professor A. Bayet of Brussels, first chairman of the International Union Against the Venereal Diseases, said (*10*): ". . . some countries . . . concentrate on the social effects . . .; others concentrate on individual treatment, aiming above all at the cure of the patient himself; others place their trust in laws and regulations, and others, without having any definite



Pan American Sanitary Bureau photograph WHO photographs

(Left) Collecting blood samples in Itaugua, Paraguay, during anti-VD campaign, 1952. (Center) Centrifuging blood samples in the field (WHO Simla, India, VD Program, 1949). (Right) A nurse in one of the teams fighting endemic syphilis in Bosnia making a blood test.

programme, do what they can here and there without any unified plan."

This diversity in methods of attacking the venereal disease problem led to the foundation of the International Union Against the Venereal Diseases. At a series of conferences organized in 1921 by the League of Red Cross Societies to discuss venereal disease, the need became apparent for establishing a forum where varying viewpoints could be aired and a measure of uniformity sought in national approaches to venereal disease control. Founded in 1923, the International Union has sought since its earliest days to aid countries represented in its membership in developing sound principles of venereal disease control. This organization has also performed useful service in publicizing venereal disease control and in stimulating public support of control efforts (*10*).

League of Nations

With creation, following World War I, of the Health Organization of the League of Nations—with greater resources and broader functions than the Office Internationale d'Hygiéne Publique—potentially effective machinery was established for a sustained global attack on health problems. The Health Organization began operating in a world where international health involved many questions other than quarantine. Among the problems faced by the young organization, for example, was that of standardizing many of the new "biologicals" and the procedures which advances in the medical sciences had produced (*8*).

Responsive to these new factors, the Health Organization of the League of Nations undertook early in its history to establish international standards for serums, biological products, and serologic reactions. Standardization was needed not only in performing serum tests for syphilis but also in interpreting and recording test results. The Health Organization of the League of Nations arranged conferences of experts in 1921, 1922, and 1923. The latter meeting and subsequent gatherings in 1928 and 1930 were working laboratory conferences, which evolved many valuable rules of serologic testing.

Standardization of antivenereal disease drugs was also part of the Health Organization's program, which embraced both arsenicals and penicillin. Provisional standards for the latter were established in 1944 (*8*).

Syphilis therapy also was studied. By the time the Health Organization came into being, arsenical treatment had gained wide acceptance among physicians. Various schemes and dosages were employed, however, and as Vonderlehr and Heller (*11*) have put it, "Almost every doctor who attained a scientific reputation in the treatment of the venereal diseases had his own plan for use of the arsphenamines." Beginning in 1928, through the agency of a Commission of Experts on Syphilis and Cognate Subjects, the Health Organization undertook an extensive inquiry into methods of treating syphilis with the arsenicals. More than 25,000 case records from clinics in Germany, Denmark, France, the United Kingdom, and the United States were analyzed. Results of the study, re-

ported in 1934, engendered widespread interest among health administrators and syphilologists.

The Brussels Agreement

The most specific accomplishment in international venereal disease control before World War II was the Brussels Agreement of 1924. The moving forces behind this convention, designed to provide venereal disease treatment facilities for merchant seamen, were the Health Organization of the League of Nations, the Office Internationale d'Hygiéne Publique, the International Labour Office, and the International Union Against the Venereal Diseases. The agreement calls for maintenance of venereal disease treatment services for seamen and watermen in the ports of signatories. This occupational group, seamen and watermen, moving from port to port and particularly subject to exposure to venereal infection, had long been looked upon as an important factor in VD epidemiology.

The Brussels Agreement was an attempt to deal with this problem in a straightforward manner. Signed on December 1, 1924, by 1938 the convention was ratified or adhered to by 56 nations, dependencies, special ports, or island groups. In practical terms, its purposes have been effectuated somewhat more broadly than the number of its adherents would indicate. For example, the United States is not a signatory; but, after passage of the Venereal Disease Control Act of 1938, foreign seamen have been permitted to obtain treatment for venereal disease in clinics organized under the act, and the clinics themselves have been included in the International Treatment Center List provided for by the agreement (*12*, *13*).

VD Control Before World War II

In a narrow sense, the record of international venereal disease control before World War II shows but few enterprises of substantial importance. Probably most valuable were the Brussels Agreement and the trailblazing done by the League of Nations in cooperative studies of syphilis serology and treatment. Beyond these specifics, however, lies the maturing of the whole concept of cooperative attacks on disease. In its modern form this concept involves the building up of an effective program of health and disease control in each nation of the world. This approach was first demonstrated by the Rockefeller Foundation, which has worked effectively since 1913 toward developing cooperative action in the health field (*14*, *15*).

To implement international cooperation as it applies to venereal infections, the early years of the 20th century produced the diagnostic and therapeutic processes which make possible the medical control of syphilis—demonstration of *Treponema pallidum*, development of the serologic test, use of the darkfield procedure in diagnosing early syphilis, and the enormous contribution of Ehrlich, salvarsan. There are, of course, a host of other factors—social, political, ethical, medical—which influence the international health movement. But those are far beyond the scope of this paper.

Principles for WHO Program

In the recommendations of the Interim Commission of the World Health Organization to the First World Health Assembly, held in Geneva in 1948, venereal disease control was among the programs assigned top priority. In selecting priorities, three principles guided the Commission (*9*): The worldwide or regional importance of the problem; the possibility of effective international action; the increased urgency of the problem as a result of war.

While there were no statistical guides by which the extent of the global venereal disease problem could be precisely assessed, data were adequate to establish the high prevalence of this group of infections and the aggravation of the problem as a result of the war. There was ample cause to believe that an international venereal disease program could be successful. Newly introduced methods of treatment, particularly penicillin, had removed many of the drawbacks of older forms of therapy; furthermore, the Interim Commission considered that, on the basis of past international experience in the field, renewed action against venereal disease was feasible. Thus, venereal disease control fitted well into the WHO plan of concentrating its initial efforts on "impact" programs. The First World Health Assembly accepted the priorities recommended by the Interim Commission, and authorized establish-

ment of expert committees in the priority areas (*8*).

WHO's venereal disease control program has been broadened since 1948 to encompass nonvenereal treponematoses (yaws, pinta, bejel). At first, the Expert Committee on Venereal Disease, mindful of its terms of reference, had recommended against bringing bejel and related spirochetoses within the scope of WHO's venereal disease control program. Although the committee recognized that these diseases merited the attention of WHO, it felt that because of the "predominantly nonvenereal nature of these conditions" (*16*) they should constitute a separate activity of the world organization. Later, however, noting the "demonstrated uniform response of various treponematoses" to penicillin (*13*), and other technical and administrative considerations, the committee gave its approval to the broader program. The Second World Health Assembly (1949) decided that an expert group on treponematoses should be established under the program projected for 1950. Following the favorable attitude of the Expert Committee on Venereal Disease as to combining treponematoses (in addition to syphilis) with the venereal disease control program, the Executive Board of WHO approved the merger of the two expert groups. The enlarged committee held its first meeting under its broadened terms of reference in August 1952.

Criteria for Broadened Program

The content and accomplishments of WHO's venereal disease and treponematoses control program are described in WHO publications and elsewhere, and no attempt will be made here to analyze them in detail. However, because this program stands at the center of today's international attack upon venereal infections, a few of the chief premises on which the program functions will be summarized:

1. WHO's approach to venereal disease control is one of public health. At its first session, the expert committee (*17*), while recognizing the "vast social implications of venereal disease," suggested that WHO concentrate on the public health and medical aspects at least "until definite plans on . . . social aspects . . . now under consideration by the United Nations and other international organizations become available."

2. One of the objectives of WHO's venereal disease control program is to help member countries establish and develop permanent control structures within national health administrations. Emphasis is placed on underdeveloped areas of high venereal disease prevalence.

3. Assistance in training venereal disease control personnel is supplied through fellowships and demonstration services and through support of training institutions in areas where facilities are limited. Demonstration teams and other phases of WHO's training program in venereal disease control are conceived as beginning points from which not only national venereal disease control programs but also broad public health programs can ultimately develop (*13*).

4. Efficient serologic testing for treponematoses is a prime requisite of an effective venereal disease control program. WHO's interest in serology is epitomized by the establishment of a Subcommittee on Serology and Laboratory Aspects (of the Expert Committee on Venereal Infections and Treponematoses) which is actively pursuing the ideal of worldwide standardization of serologic procedure, technique, and reporting of results in serum tests for treponematoses. Both the parent group and the subcommittee have emphasized the advantages of the cardiolipin and lecithin antigens in serologic testing. Through the cooperation of the Expert Committee on Biological Standardization, international reference preparations of these antigen components have been deposited with the Standards Department of the State Serum Institute, Copenhagen, and a standard description of them has been included in the International Pharmacopoeia. Several countries in Europe have begun to produce these substances, and there are plans for similar steps in Southeast Asia and in the Americas (in addition to the United States, where cardiolipin and lecithin antigens were first developed) (*17*, *18*).

5. Penicillin therapy is in general use in WHO-sponsored programs of treponemal disease control. While the problem of penicillin production and distribution was separated from the venereal disease program by the First World Health Assembly, the expert committee has

watched the subject with great interest and concern. In fact, at its second session in 1948 the committee observed that in its opinion (*16*), " . . . the limited availability of penicillin [was] the outstanding restricting factor in venereal disease control in the world today." The economic commissions of the United Nations and WHO have worked together to stimulate production of penicillin, and the antibiotic is becoming somewhat more accessible for worldwide use. A Section on Antibiotics has been created within the WHO Secretariat, reflecting the importance with which this subject is viewed within the organization (*13*).

6. One of the great needs of the world in venereal disease control is the exchange of scientific information on venereal disease among professional workers. To aid in meeting this need, WHO has prepared a number of technical documents from data collected from many parts of the world. Another manner of meeting this need is through international meetings of experts and other workers. For example, in 1950, an International Symposium on Syphilis was held in Helsinki, Finland, through the cooperation with WHO of the Finnish and French health administrations. In March 1952, the First International Symposium on Yaws was held in Bangkok, in an effort to draw together the experience and thinking of professional workers on a disease which exists widely in Africa, Asia, certain of the Pacific Islands, and parts of the Americas.

7. The maritime aspects of venereal disease control have been studied by WHO from its earliest days. At its first session in 1948, the expert committee considered the view expressed by the Economic and Social Council of the United Nations that diplomatic conventions in technical fields should be replaced by health regulations adopted by the World Health Assembly. In 1949, at its third session the committee, having noted that delays are unavoidable in developing such regulations, pointed out the importance of the Brussels Agreement as the "sole practical instrument for venereal disease control between countries" (*13*, *17*).

A particular segment of the maritime venereal disease problem has been attacked by the International Anti-Venereal Disease Commission of the Rhine. After discussion between WHO and the governments of Belgium, the Netherlands, France, Germany, and Switzerland, the Commission was established in 1951 to coordinate venereal disease services of these five nations for the benefit of the Rhine River boatmen and their families—a floating population of some 45,000 persons—and to establish diagnostic and treatment facilities in the principal ports of the river. An extension of the Commission's work is the Port Demonstration Project, established in Rotterdam to study venereal disease control among seafarers.

8. As units of a global structure, regional health organizations have been established to serve the needs of particular areas. The regional system of WHO was completed in 1951. There are today six regional offices covering Africa, the Americas, the Eastern Mediterranean, Europe, Southeast Asia, and the Western Pacific. The Regional Office of the Americas has been established in the Pan American Sanitary Bureau in Washington.

PASB and WHO Projects

Actually, the PASB has a far longer history in international health than WHO. The first health agency to function over a wide area for many governments, it antedates the Office Internationale d'Hygiéne Publique by several years, having been formally organized by the Pan American Sanitary Conference in 1902. It functions today both as WHO's regional office and independently as the operating agency of the Pan American Sanitary Organization (*8*, *9*).

A number of WHO-sponsored or -aided venereal disease control projects have been and are being conducted in the Americas. A yaws-eradication program in Haiti, for example, is being conducted under an agreement between PASB (as WHO's regional office), United Nations International Children's Emergency Fund, and the Haitian Government. Numerous South American countries have some kind of WHO-aided venereal disease control projects in progress, for example, demonstration and training projects in Ecuador and Paraguay, a training center in Venezuela, and laboratory training programs in Guatemala and Brazil.

WHO photographs

(Left) WHO public health educator calls a conference of social workers from Gabiah Province, Egypt, during a campaign against congenital syphilis. (Right) Director of Health at Sarajevo and leader of the Yugoslav-WHO-UNICEF antiepidemic syphilis campaign in Bosnia, examines boy's mouth for syphilitic lesions.

A number of other cooperative venereal disease control operations have been conducted in Mexico, Central America, and South America, through bilateral planning between the United States and other individual governments. And during World War II, the Inter-American Cooperative Health Program was initiated among the American Republics not only to provide medical and public health services for war workers but also to supplement and extend long-term disease control programs. Functioning through the Institute of Inter-American Affairs and the governments concerned, this program included VD control operations. At present, the Institute is cooperating with the Mexican Government and the Pan American Sanitary Bureau in a VD control program along the Mexico-United States border (*19*).

The PHS and the International Program

The Public Health Service entered the international venereal disease control picture through the League of Nations clinical studies of syphilotherapy. Requested to participate in these studies, the Public Health Service undertook to assemble 10,000 case records from syphilis clinics in the United States, to analyze them, and to forward the records to the League for further analysis and comparison with data from other countries. Incidentally, at the time the League studies were begun, the Service decided to utilize the same sources of data in the United States for a more intensive investigation of the results of treatment of syphilis in this country. The participants in this inquiry—leading syphilis clinics—were the first members of the Cooperative Clinical Group, which developed some of the most comprehensive statistical and clinical studies of syphilis treatment on record.

The United States venereal disease control program, through its successful application of public health techniques to the venereal disease problem, has influenced the structure and content of WHO's antivenereal disease activities. In 1949, a seven-member Syphilis Study Commission of WHO toured venereal disease control

installations in this country (*a*) to evaluate methods in use in the United States and the importance of these methods in national and international programs, and (*b*) to study control methods, particularly penicillin treatment in syphilis. The Commission reported the organization and methods in the United States to be a helpful guide in planning future programs in other parts of the world, subject, of course, to adaptations to meet local conditions and problems.

Standardized laboratory procedures in the United States program and methods employed in compiling and analyzing statistical data were approved. Certain features of training and utilization of personnel were also viewed with favor, for example, special training in venereal disease control for medical officers assigned to this field, and performance by specially trained nurses, health educators, and investigators of a major part of epidemiological, educational, and technical work (*20*).

Undoubtedly, the experience in the United States with penicillin has hastened acceptance of this form of therapy in the international program. The WHO Syphilis Study Commission thought that the drug used in a control program is less important in diminishing the amount of venereal disease than the ready availability of treatment facilities plus an active case-finding program. Nevertheless, it recognized that the rapidity and nontoxicity of penicillin therapy makes this antibiotic of great value in syphilis control.

Results of WHO's Program

One of the most significant undertakings of WHO in treponemal disease control, in terms of permanent progress, is the training phase of the program. Personnel are being indoctrinated in essentials of public health practice which will serve both specialized treponemal disease campaigns and generalized health programs. For the private physician in contact with epidemiological and treatment demonstrations, there is opportunity to learn some of the attitudes and substance of preventive medicine—particularly important in areas where physicians receive little of these in their medical training.

Some valuable lessons in the methodology of mass attacks on disease are emerging. Clark (*21*) has pointed out the contribution to epidemiology made by the endemic syphilis program in Bosnia, Yugoslavia. Reynolds and Guthe (*22*) have summarized conclusions on case finding and treatment reached in WHO's early programs of mass penicillin therapy. These and other experiences indicate that in mass treatment programs a very high percentage of the population involved must be reached for examination if results are to be satisfactory. Experience in Haiti has given some excellent leads as to how this high level of coverage may be obtained. Where reliance is placed on voluntary clinic attendance, even when bolstered by a public appeal campaign, less than half the population will be reached. When, in addition, mobile clinics are used in strategic areas, the percentage rises to 70. Ninety-percent coverage in Haiti was achieved only when a house-to-house survey was employed.

Towering above all other results, real or potential, of international treponemal and venereal disease control is the prospect that the massive prevalence of these diseases may be cut down and possibly eradicated in large areas. Both in terms of humanitarian objectives and of economic improvement of the areas involved, this prospect has very broad ramifications indeed.

It has been pointed out that treatment alone has never eradicated a disease on a global scale; neither has vaccination nor environmental sanitation. But history abounds with instances of disease controlled by public health methods, and WHO's experience with mass treatment of venereal and treponemal disease encourages the belief that control and possibly eradication of these infections can be achieved.

This experience shows that infectiousness in treponematoses can be significantly reduced by mass use of penicillin in aluminum monostearate. In the Bosnia program, cases of secondary syphilis were found at the first control examination to be about 10 percent of the number found at the beginning of the campaign. At later examinations, this number was further reduced. While results are less spectacular in

other campaigns, significant reductions in infectious cases have occurred in programs in Haiti, Indonesia, Thailand, and Iraq. Up to January 1953, well over 9,000,000 persons had been examined and over 3,000,000 treated for treponemal disease in intensive campaigns sponsored by WHO and often substantially aided by UNICEF (*22*).

A single mass treatment campaign in an area is not sufficient to master permanently the venereal or treponemal disease problem in that area. Successful public health programs are usually protracted affairs. In treponemal and venereal disease, there must be a continuing effort to decrease the number of infectious cases, and resurveys are necessary to prevent recrudescence. Many factors—extent of the disease, completeness of case finding, opportunities for reintroduction—must be considered before the question of how many mass surveys can be answered for an area. Infectious cases must be brought down to the point where the local case-finding and treatment operation is adequate to deal with remaining pockets of infectious cases. Clearly, the more mature and complete the local public health organization, the earlier it can assume full responsibility for the local disease situation.

This fact helps to illuminate the wisdom of WHO's approach to venereal and treponemal disease control: to aid, to the extent of its resources, in the immediate diminution of disease in areas of greatest need, and at the same time to assist in building permanent public health structures especially through training of native personnel. This kind of attack, well supported and continuous, makes bright the hope that effective worldwide control of venereal and treponemal disease can be accomplished.

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